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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,327	06/06/2001	David S. Millington	5405-230	7519

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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
COLE, MONIQUE T	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 03/24/2004

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,327	MILLINGTON ET AL.	
	Examiner	Art Unit	
	Monique T. Cole	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,26-40,43,44,46 and 48-52* is/are rejected.

7)☒ Claim(s) *24,25,41,42,45,47,53 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 23 recites the limitation "the oligosaccharides". There is insufficient antecedent basis for this limitation in the claim.

3. Claims 46 & 52 recite the limitation "said quantifying step" in claim 43. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-7, 9,10, 14-21, 26-30, 32 & 33 rejected under 35 U.S.C. 102(b) as being anticipated by "*Increased Urinary Excretion of a Glycogen-Derived Tetrasaccharide in Heterozygotes with Glycogen Storage Diseases Type II and III*" from the Lancet (herein referred to as "Lancet"). Lancet teaches a method of screening a subject for glycogen storage disease that comprises determining the level of Glc_4 as a marker indicative of the presence of the disease. The rate of excretion of Glc_4 is greater in clinical conditions such as glycogen storage disease II and III. Urinary specimens were used to gauge the amount of the marker and the Glc_4 level was

determined using such quantitative methods as radioimmunoassay, gas chromatography and mass spectrometry. The Glc_4 of those with glycogen storage disease was compared against normal individuals and a reference value was obtained that is indicative of the likelihood of glycogen storage disease.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 8 & 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet.

Lancet teaches the invention substantially as claimed with the exception of expressly teaching that the subject of Glc_4 is a neonate.

However, Lancet does teach that Glc_4 can be detected in prenatal fetuses as well as patients that range in age from 5-20 years. Thus, given the fact that the marker can be detected

prior to birth and later in the child's life, it would have been obvious to one having ordinary skill in the art to expect that the marker could also be detected when the subject is an infant, absent any evidence of unexpected or superior results.

6. Claims 11 & 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet as applied to claims 1-10, 14-21, 26-30, 32 & 33 above, and further in view of *"Evaluation of the lysosome-associated membrane protein LAMP-2 as a marker for lysosomal storage disorders"* by Hua et al. (herein referred to as "Hua") & USP 5,252,489 to Macri (herein referred to as "Macri").

Lancet, as applied above, fails to teach that blood is used as a sample for testing for the Glc_4 marker or that the blood sample is dried.

Hua teaches that it is known in the art to use neonatal blood samples when testing for markers indicative of lysosomal storage disorder, a class of disorder in which Pompe disease is included. In the absence of a family history, presymptomatic detection can be achieved only by a comprehensive newborn screening program.

It would have been obvious to one having ordinary skill in the art to use neonatal blood as sample means of detecting Glc_4 or other markers implicated in the development of lysosomal storage disorders because blood is routinely taken from infants at the time of their birth for PKU testing and it would be efficient to use the same blood sample to screen for other metabolic diseases. Neonatal blood screening is less invasive and more readily accessible at the time of birth, making it easier to obtain and screen multiple samples.

With regard to dried blood samples, the motivation for using dried blood samples is expressly provided in Macri. Macri teaches that use of dried samples, whether they be blood or

urine, have the advantages of: being able to be stored for analysis or transport at a later time, preventing contamination by avoiding the cumbersome transportation techniques of liquid test tube handling and avoiding the medical hazards associated with liquid sample splashes, needle sticks and broken test tubes. See col. 3, lines 16-52 & col. 4, lines 3-12. Thus, given the noted advantages that Macri provides for using dried test samples in lieu of liquid samples, it would have been obvious to one of ordinary skill in the art to modify the screening method of Lancet to include dried blood samples as taught in both Hua and Macri.

7. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet as applied to claims 1-10, 14-21, 26-30, 32 & 33 above, and further in view of USP 5,252,489 to Macri (herein referred to as "Macri").

Lancet, as applied above, fails to teach that the urine test sample is dried.

However, Macri teaches that use of dried samples, whether they be blood or urine, have the advantages of: being able to be stored for analysis or transport at a later time, preventing contamination by avoiding the cumbersome transportation techniques of liquid test tube handling and avoiding the medical hazards associated with liquid sample splashes, needle sticks and broken test tubes. See col. 3, lines 16-52 & col. 4, lines 3-12. Thus, given the noted advantages that Macri provides for using dried test samples in lieu of liquid samples, it would have been obvious to one of ordinary skill in the art to modify the screening method of Lancet to include dried urine samples as taught in Macri.

8. Claims 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet in view of *"Clinical and Metabolic Correction of Pompe Diesease by Enzyme Therapy in Acid Maltase-deficient Quail"* by Kikuchi et al. (herein referred to as "Kikuchi").

Lancet, as discussed above, does not teach that the subject is undergoing treatment for Pompe disease.

Kikuchi teaches that enzyme replacement therapy is the latest in a series of therapies for the treatment of Pompe disease.

Thus, it would have been obvious to one having ordinary skill in the art to expect that some form of treatment would be provided for those suffering from the potentially fatal Pompe disease. As enzyme replacement therapy is the latest and most promising therapy for this disorder, it would be expected that this treatment would be utilized for those persons whose cases were thought to be terminal. Moreover, any patient undergoing treatment for a disease as serious as Pompe disease would most certainly be under the care of a physician and would be monitored carefully for any changes in their condition so that the therapeutic regimen could be adjusted accordingly.

9. Claims 22, 43, 44 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet as applied to claims 1-7, 9, 10, 14-21, 26-30, 32 & 33 above, and further in view of *"The analysis of diagnostic markers of genetic disorders in human blood and urine using tandem mass spectrometry with liquid secondary ion mass spectrometry"* by Millington et al. (herein referred to as "Millington").

Lancet, as applied above, fails to teach that Glc_4 is quantified by tandem mass spectrometry. Instead, Lancet teaches using gas chromatography-mass spectrometry.

Millington, however, teaches that it is beneficial to use tandem mass spectrometry as an alternative to gas chromatography-mass spectrometry because it is time-saving, has greater accuracy and it has the capability for automation necessary for large-scale neonatal screening of inborn errors of metabolism. Thus, given the aforementioned advantages of tandem mass spectrometry taught by Millington, it would have been obvious to one having ordinary skill in the art to modify the quantification method of Lancet to use tandem mass spectrometry when testing urine samples for Glc_4.

10. Claims 39, 40, 49 & 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lancet, Hua and Macri as applied to claims 11 & 12 above, and further in view of Millington.

Lancet, Hua and Macri, as applied above, fail to teach that Glc_4 is quantified by tandem mass spectrometry. Instead, Lancet teaches using gas chromatography-mass spectrometry.

Millington, however, teaches that it is beneficial to use tandem mass spectrometry as an alternative to gas chromatography-mass spectrometry because it is time-saving, has greater accuracy and it has the capability for automation necessary for large-scale neonatal screening of inborn errors of metabolism. Thus, given the aforementioned advantages of tandem mass spectrometry taught by Millington, it would have been obvious to one having ordinary skill in the art to modify the quantification method of Lancet, Hua and Macri to instead use tandem mass spectrometry when testing blood samples for Glc_4.

11. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lancet as applied to claims 8 & 31 above, and further in view of Millington.

Lancet, as applied above, does not that Glc_4 is quantified by tandem mass spectrometry. Instead, Lancet teaches using gas chromatography-mass spectrometry.

Millington, however, teaches that it is beneficial to use tandem mass spectrometry as an alternative to gas chromatography-mass spectrometry because it is time-saving, has greater accuracy and it has the capability for automation necessary for large-scale neonatal screening of inborn errors of metabolism. Thus, given the aforementioned advantages of tandem mass spectrometry taught by Millington, it would have been obvious to one having ordinary skill in the art to modify the quantification method of Lancet to instead use tandem mass spectrometry when testing urine samples for Glc_4.

Allowable Subject Matter

12. Claims 24, 25, 41, 42, 45,47, 53, 54 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. Claims 23, 46 and 52 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

14. The following is a statement of reasons for the indication of allowable subject matter: the prior art does not teach or reasonably suggest a process for screening a subject for Pompe disease wherein the hexose tetrasaccharide is derivatized with butyl-para-aminobenzoic acid prior to

quantification by tandem mass spectrometry or that the quantification by tandem mass spectrometry is standardized using a [U-^{13}C] glucose labeled hexose tetramer as an internal standard.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monique T. Cole whose telephone number is 571-272-1255. The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Monique T. Cole
Examiner
Art Unit 1743

MC